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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,700	09/25/2003	Masahiro Kajiwara	6854-24-1	6367

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FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

EXAMINER	
SEAMAN, D MARGARET M	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 08/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/669,700	KAJIWARA, MASAHIRO	
	Examiner	Art Unit	
	D. Margaret Seaman	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application was filed 9/25/2003 and is a DIV of 10/220803 (filed 9/5/2002, ABN) which is a 371 of PCT/JP01/01618 (3/2/2001) which claims foreign priority to JP 2000-62012 (3/7/2000). RCE papers were filed 6/20/2005. Claims 1-8 have been canceled by paper dated 6/20/2005. Claims 9-16 are before the Examiner.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 9-16 remain rejected under 35 U.S.C. 102(b) as being anticipated by Hirai (JP 04077476). The rejection is maintained for reasons of record.

Applicants argues that since Hirai fails to teach the treatment of ulcers by inhibiting urease or H. Pylori activity, then the rejection falls. For inherency to stand, the same patient population must be treated. The first page of the specification states

> Urea secreted from the gastric parietal is hydrolyzed by urease to produce ammonia and carbon dioxide. Ammonia has a strong mucosa injurious effect, thereby to cause a blood flow disorder of the gastric mucosa, and also neutralizes gastric acid, thereby to enable habitation of Helicobacter pylori within the stomach under a severe acidic environment. In case Helicobacter pylori adheres to the gastric mucosa, epithelial cells of the gastric mucosa produce Interleukin-8 (IL-8) as a kind of cytokines, while IL-8 acts on neutrophils, thereby to cause migration and activation of neutrophils. The activated neutrophils form phagocytosis and phagosome and also cause production of active oxygen and degranulation. The produced active oxygen itself causes a mucosa injury and induced to hypochlorous acid through an action of chlorine and myeloperoxidase in the stomach, and is also converted into monochloramine by means of ammonia, thus causing a cell injury.

The bacteria (H.Pylori) starts a chain reaction which creates high acidity in the stomach. This high level of acidity damages the mucosa. The ulcer is caused by this damaged mucosa. The compounds used in the instant method claims therefore treat the high levels of acid in the stomach and allow the ulcer to heal. To treat the bacterial infection, (see page 15 of the instant specification) coadministeration of the compounds of formula (1) with other active ingredients such as antibiotics must be done. The antibiotics treat the bacterial infection and the compounds of formula (1) treat the high levels of acid. Due to this, the same patient population is being treated by the same compound as

taught by the prior art. Therefore, the instant method claims are inherently taught by the prior art.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 9-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant specification does not adequately describe the nexus between the modulation of the urease activity and a useful treatment of a disease/condition. Modulation of a receptor involves antagonism, inhibition, agonism and others. These modulations are sometimes opposite reactions to the same receptor. It is not seen where the instant specification adequately describes the nexus between the modulation of the urease activity and a useful treatment of a single disease or condition. The instant method of inhibiting a urease activity or inhibiting a Helicobacter pylori activity reaches out to as yet unidentified conditions/ activities/disorders, the description of which are not found in the specification.

5. Claims 9-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims,
2) The nature of the invention,
3) The state of the prior art,
4) The level of one of ordinary skill,
5) The level of predictability in the art,
6) The amount of direction provided by the inventor,
7) The existence of working examples,
8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The nature of the invention: The nature of the invention is the method of treating a disorder that is modulated urease.

The state of the prior art: The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to the therapeutic effects of all diseases, whether or not the modulation of urease would make a difference in the disease. Hence, in the absence of a showing of a nexus between any and all known diseases and the modulation of urease, one of ordinary skill in the art is unable to fully predict possible results from the administration or coadministeration with another active ingredient of the compound of formula 1 due to the unpredictability of the role of modulation of urease.

The presence or absence of working examples: The compounds of formula (1) have been shown to inhibit urease. However, the specification does not provide the

treatment of any gastric mucosa injury caused by urease. The specification does not specify what all is encompassed by gastric mucosa injury other than ulcers.

The amount of direction or guidance present: The guidance present in the specification is that of the compounds work to treat any and all disease/conditions that are linked to gastric mucosa injury. However, the specification does not state what are all the conditions that are covered by gastric mucosa injury. Due to this, very little guidance as to why to use the instant methods is given by the instant specification.

The breadth of the claims: The claims are drawn to the treatment of any and all diseases that are treatable by treating gastric mucosa injury caused by urease. However, the only condition linked by the instant specification to this is ulcers.

The quantity of experimentation needed: The quantity of experimentation needed is undue. One skilled in the art would need to determine what diseases/conditions out of all known diseases/conditions would be benefited by the mediation of urease by gastric mucosa injury and then which of the claimed compounds would provide treatment of the disease/condition.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compounds of claim 1 for the treatment of any disease. As a result necessitating one of ordinary skill to perform an exhaustive search for which diseases can be treated by which compound of claim 1 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

The court holds that claims directed to mediating a biological pathway are devoid identifiable utility and are therefore not useful. Unless the pathway at issue is critical to treating some condition and the pathway modification and disease treatment are inexorably linked, such pathway modification is devoid of utility.

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, one of ordinary skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compounds of the instant claims, with no assurance of success.

This rejection can be overcome by deleting the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. Margaret Seaman whose telephone number is 571-272-0694. The examiner can normally be reached on 630am-4pm, First Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecelia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

D. Margaret Seaman
Primary Examiner
Art Unit 1625

dms